ANNALS OF SURGERY
Vol. 227, No. 6, 800–811

Surgical Treatment of Adenocarcinoma of the Rectum

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Objective

The authors' aim was to determine survival and recurrence rates in patients undergoing resection of rectal cancer achieved by abdominoperineal resection (APR), coloanal anastomosis (CAA), and anterior resection (AR) without adjuvant therapy.

Summary Background Data

The surgery of rectal cancer is controversial; so, too, is its adjuvant management. Questions such as preoperative *versus* postoperative radiation *versus* no radiation are key. An approach in which the entire mesorectum is excised has been proposed as yielding low recurrence rates.

Methods

Of 1423 patients with resected rectal cancers, 491 patients were excluded, leaving 932 with a primary adenocarcinoma of the rectum treated at Mayo. Eighty-six percent were resected for cure. Surgery plus adjuvant treatment was performed in 418, surgery alone in 514. These 514 patients are the subject of this review. Among the 514 patients who underwent surgery alone, APR was performed in 169, CAA in 19, AR in 272, and other procedures in 54. Eighty-seven percent of patients were operated on with curative intent. The mean follow-up was 5.6 years; follow-up was complete in 92%.

APR and CAA were performed excising the envelope of rectal mesentery posteriorly and the supporting tissues laterally from the sacral promontory to the pelvic floor. AR was performed using an appropriately wide rectal mesentery resection technique if the tumor was high; if the tumor was in the middle or low rectum, all mesentery was resected. The mean distal margin achieved by AR was 3 ± 2 cm.

Results

Mortality was 2% (12 of 514). Anastomotic leaks after AR occurred in 5% (16 of 291) and overall transient urinary retention in 15%. Eleven percent of patients had a wound infection (abdominal and perineal wound, 30-day, purulence, or cellulitis). The local recurrence and 5-year disease-free survival rates were 7% and 78%, respectively, after AR; 6% and 83%, respectively, after CAA; and 4% and 80%, respectively, after APR. Patients with stage III disease, had a 60% disease-free survival rate.

Conclusions

Complete resection of the envelope of supporting tissues about the rectum during APR, CAA, and AR when tumors were low in the rectum is associated with low mortality, low morbidity, low local recurrence, and good 5-year survival rates. Appropriate "tumor-specific" mesorectal excision during AR when the tumor is high in the rectum is likewise consistent with a low rate of local recurrence and good long-term survival. However, the overall failure rate of 40% in stage III disease (which is independent of surgical technique) means that surgical approaches alone are not sufficient to achieve better long-term survival rates.

Surgery for carcinoma of the rectum remains the one treatment modality offering a chance of cure. Each generation of surgeons has debated the best operation to perform for rectal cancer, with choices based largely on outcome analysis; prospective trials proposing to solve surgical dilemmas in rectal cancer are easily conceived but rarely performed.

In addition to technical maneuvers, adjuvant therapy has evolved to complement the effectiveness of surgery; indeed, it now plays a significant and life-enhancing role in the overall approach to the patient with rectal cancer, depending on stage.

Presented at the 109th Annual Meeting of the Southern Surgical Association, November 30 to December 3, 1997, The Homestead, Hot Springs, Virginia.

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Accepted for publication December 1997.

Several authors have documented that technical excellence and the incidence of local recurrence are linked tightly. Because local recurrence rates have been high in some series, prospective trials of adjuvant management have been instituted in an attempt to salvage surgical outcomes.[1–3] Such trials all show significant improvement in local recurrence and survival rates in patients treated with chemoradiation therapy *versus* either surgery alone or radiation alone, but the underlying benefit appears to depend on the presence of a high recurrence rate after surgery alone. Decreasing the local recurrence rate from 20% or 30%[1] is important, but the utility of trying to decrease it from 5% may be an entirely different matter.

Heald and Ryall,[4] MacFarlane et al.,[5] and Enker et al.[6] have contributed to the most recent technical debate. Local recurrence in the range of 4% to 8% has been reported using an operation termed "total mesorectal excision." These results have inspired these authors and others to claim that total mesorectal excision is the management standard for rectal cancer. We were especially interested in this technique in light of the results from our institution, reported by Wilson and Beahrs[7] 22 years ago, that the local recurrence rate after anterior resection (AR) was only 8%, but without the increased morbidity reportedly accompanying total mesorectal excision.[5] The techniques used in the patients reported by Wilson and Beahrs included appropriate bowel and mesorectal margins achieved by resecting the envelope of rectal mesentery and supporting tissues for a distance of 5 cm below high rectal tumors; for middle and low tumors, the entire mesorectum posteriorly and the supporting structures laterally were excised and the anastomosis was constructed just above the pelvic floor. The same approach was used for coloanal anastomosis (CAA) and for abdominoperineal resection (APR).

Our aim was to determine the local recurrence rate and the 5-year survival rate in patients in whom primary adenocarcinoma of the rectum was resected using these surgical principles and in whom no adjuvant therapy was performed.

MATERIALS AND METHODS

The medical records of 1423 consecutive patients diagnosed with rectal carcinoma during the period 1982 to 1989 were reviewed. The following criteria eliminated 491 patients from further evaluation: transanal or posterior excision for nonmetastatic disease (133 patients), recurrent disease (105 patients), primary treatment elsewhere (101 patients), history of another primary tumor within 4 years of treatment for rectal carcinoma (55 patients), carcinoma *in situ* (97 patients). Adjuvant therapy (usually a combination of chemotherapy and radiation) was administered to an additional 418 patients; because of the heterogeneity of the treatments performed and because we were interested in the results of surgery alone, these patients were likewise excluded from further evaluation. The total number of patients excluded, therefore, was 909. The remaining 514 patients with primary, invasive adenocarcinoma of the rectum and rectosigmoid treated for cure by surgery alone at Mayo Clinic made up the target population.

Definitions

Tumor size was documented as the longest diameter of the tumor on gross examination of the fresh specimen. Invasion of adjacent organs and lymph node metastasis were proven histologically. The location of the tumor was measured in distance (centimeters) from the dentate line, and the measurements were made by the physician at the time of diagnosis. In the few patients in whom this information was unavailable and APR was performed, the gross pathologic specimen was used to determine the distance from the dentate. Tumors were classified as low rectal, middle rectal, high rectal, and rectosigmoid if they were 0 to 5 cm, 6 to 10 cm, 11 to 15 cm, and >15 cm from the dentate line, respectively. The distal mucosal margin after resection was recorded by the pathologist on the fresh specimen where applicable.

Operative procedures were curative if all the macroscopic disease was removed at the time of surgery. Procedures were palliative when there was evidence of gross residual disease at the end of surgery.

Postoperative mortality was defined as death occurring in the hospital or within 30 days of the primary operative procedure. In-hospital complications were defined as those that occurred during the hospital stay for the primary treatment; postdischarge complications were defined as those that occurred thereafter. The criteria for labeling a wound as infected were liberal: purulent discharge with opening of the wound, serous discharge with opening of the wound or antibiotic administration, and cellulitis with administration of antibiotics.

Follow-Up

Questionnaires were sent to all patients who had an incomplete follow-up. After two mailings, either the patient or the local physician was contacted by phone. Patients were followed until death or within 1 year of data collection. Follow-up was complete in 92% (468 of 514) of the patients. Median follow-up was 5.6 years (range 1 to 13) for patients alive at the conclusion of the study.

End Points

The end points of the study were survival and recurrence at final follow-up. The criteria for establishing recurrent disease were histologic confirmation, palpable disease or disease evident on radiographic studies with subsequent clinical progression, and supportive biochemical data (*e.g.*, rising level of carcinoembryonic antigen).

Overall survival was defined as the time from the date of primary treatment to the date of death. Patients who died in

the postoperative period were included in survival analysis. Disease-free survival was defined as the time from the date of primary treatment to the date of first recurrence. The probability of recurrence was the reciprocal of the disease-free survival and represents the chance of developing the first recurrence at 5 years.

Patients with recurrence were defined in terms of local or distant recurrence. Local recurrence was confined to the rectum, pelvis, or adjacent organs; otherwise, the recurrence was labeled as distant. Because surgical technique is theoretically limited to controlling disease in the region of the primary tumor, the "local only" pattern was the cumulative probability of developing only local recurrence at 5 years. These patients did not develop distant recurrences and theoretically were pure surgical failures.

Staging System

Survival rates, rates of disease-free survival, probability of recurrence, and patterns of local recurrence were calculated using the TNM staging system. The UICC/AJC colorectal staging system uses three staging variables. Primary tumor (T) was classified in four classes: T1, primary tumor invades submucosa; T2, primary tumor invades muscularis propria; T3, primary tumor invades through muscularis propria into the subserosa or into nonperitonealized pericolic or perirectal tissues; and T4, primary tumor invades other organs or structures. The regional lymph node (N) variable was classified into four classes also: N0, no nodal involvement; N1, one to three perirectal or pericolic nodes involved; N2, four or more perirectal or pericolic nodes involved; and N3, metastasis in any lymph node along the course of a named vascular trunk. The distant metastasis (M) was classified in two classes: M0, no metastasis, and M1, distant metastasis. Stage groupings were as follows: stage I, T1 or T2 tumor with no nodal involvement or distant metastasis; stage II, T3, or T4 primary with no nodal involvement or distant metastasis; stage III, any type of primary tumor with nodal involvement but no distant metastasis; and stage IV, any type of primary tumor or regional lymph nodes with distant metastasis.

Surgical Procedures

Operations performed included 169 APRs, 272 low ARs, 19 CAAs, and 54 other procedures. Most of the "other" procedures were Hartmann procedures for stage IV rectal cancer. The other major procedure was proctocolectomy and ileorectostomy for ulcerative colitis complicated by a rectal cancer.

The mean distal mucosal margin (measured in the pathology laboratory) was 3.2 cm (SD 1.8). The choice of operative procedure depended on the location of the tumor from the dentate line and stage. Most of the APRs and CAAs were done for distal tumors; low AR and modified Hartmann's procedures were commonly done for more proximal tumors.

The sigmoid colon was first mobilized by incising along the left lateral border. Splenic flexure mobilization was performed when needed to achieve a tension-free anastomosis in the pelvis. The peritoneal reflection was then opened widely. The sigmoid was retracted anteriorly and the inferior mesenteric vessels were identified, ligated, and divided at the level of the left colic artery. Attention was then directed to the area of the sacral promontory, where the presacral space was entered and the presacral nerves were preserved. As the avascular presacral space was developed sharply and Waldeyer's fascia incised sharply, care was taken never to enter the mesentery of the rectum.

For tumors in the upper third of the rectum, dissection was carried at least 5 cm below the tumor. Lateral dissection was performed at the sidewalls of the pelvis. Dissections were not "coned"—that is, the envelope of supporting structures about the rectum were dissected in a square to at least 5 cm below the tumor. Anteriorly, the vagina or prostate was mobilized off the rectum by alternating sharp and gentle blunt dissection.

For tumors at the middle or lower third of the rectum, the entire mesorectum was mobilized to the pelvic floor in the avascular plane. The rectum was elevated and transected and an anastomosis was constructed (hand or stapled) 2 to 4 cm above the levators, depending on the tumor location. CAA was performed in exactly the same manner, but in patients in whom the tumor was too low to allow reanastomosis of rectum to colon. The abdominal portion of the APR was performed using exactly the same technique as for low AR and CAA, except the rectum was not transacted and the anus and rectum were widely excised from below.

Statistical Analyses

Multivariate analysis performed to identify independent determinants of survival and recurrence was done using the following clinicopathologic variables: age, sex, presence of a comorbid condition, presence of symptoms, size of tumor, histologic grade of tumor, depth of penetration of tumor, lymph node involvement, metastatic status, and type of operative procedure done.

Data are presented as median (range) or mean (standard deviation). The product-limit method (Kaplan–Meier) was used to analyze the survival and patterns of recurrence. The two-tailed log-rank test was used to assess differences between numbers. All the risk factors for their effect on overall survival and probability of recurrence were first analyzed univariately, and the statistically significant variables were used to construct a multivariate model using the Cox proportional hazards method. Interactions were also analyzed to confirm independence.

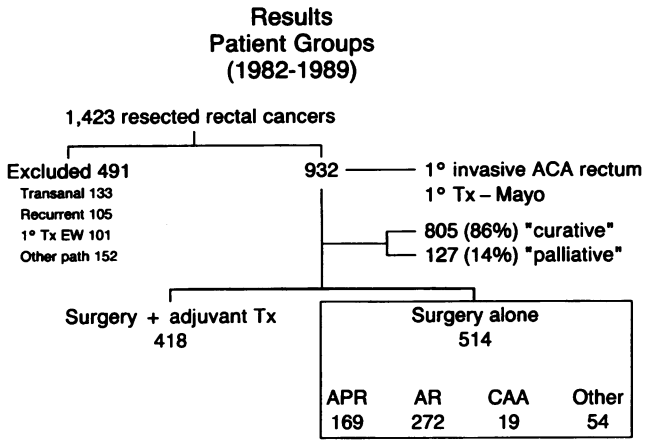

Figure 1. Flow diagram of patient populations studied.

RESULTS

Patient Population

The target population consisted of 514 patients (Fig. 1). Resection with curative intent was carried out in 446 patients (87%); 68 patients (13%) had palliative procedures. The patients treated palliatively included 6 with locally advanced disease (2 with stage B, 4 with stage C) and 62 (12.8% of total) with distant metastasis. Information on the disease status was available for 495 patients of the 514 patients undergoing curative resections. An additional 19 patients were excluded only while doing the Kaplan–Meier analysis or type of recurrence analysis because the date of recurrence (2 patients), the type of recurrence (4 patients), or both (13 patients) were missing.

The median age of the group was 67 years (range 23 to 99). There were 316 men and 198 women. Comorbid conditions were present in 60% of patients, hypertension and diabetes being the most common (Table 1). Symptoms were present in 83% of the patients at presentation. Bleeding per rectum was the most common symptom, followed by change in bowel habits, pain, and weight loss (>10 lb) (Table 2). Six patients had symptoms and signs of large bowel obstruction. The median duration of symptoms was 3 months (range 0.25 to 60). No symptoms were present in 16% of the patients and the diagnosis was made during routine performance of colonic roentgenography or proctoscopy.

Tumor Characteristics

The median tumor size was 4.2 cm (range 0.25 to 13). There were 204 (40%) tumors in the lower third, 209 (41%) in the middle third, and 70 (19%) in the upper third of the rectum. Sixteen tumors (3%) were in the rectosigmoid region. In the remaining 15 patients (3%), the distance from the dentate line was unavailable. All tumors were primary adenocarcinomas on histology. Two percent of tumors were Broder's grade 1, 79% grade 2, 17% grade 3, and 2% grade 4.

Stages

Lymph nodes were histologically free of tumor in 395 patients; 102 had tumor-positive nodes. The median number of nodes involved was 2 (range 1 to 29). In 17 patients, the nodes were not evaluated histologically, but all these patients had distant metastasis and thus stage D disease. There were 272 stage I, 111 stage II, 63 stage III, and 68 stage IV patients. Twenty-five patients had histologically proven tumor invasion to adjacent structures (stage B, 8; stage C, 6; stage D, 11) at surgery. The pelvic sidewall was the most common structure invaded, followed by the urinary bladder. The liver was the most commonly involved organ in stage D disease.

Mortality and Morbidity

The overall 30-day postoperative mortality rate was 2.3% (12 of 514). Ten of the 12 deaths were caused by cardiopulmonary complications. No patient died from complications of an anastomotic leak or of pelvic sepsis. The mortality rates for stage A, B, C, and D were 0.4%, 0.9%, 6.3%, and 8.8%, respectively. Patients undergoing Hartmann's procedure had the highest mortality rate (18.7%), and all but one of these patients had stage D disease. The mortality rate was 1.8% for APR and 1.1% for low AR.

The overall in-hospital complication rate was 46% (Table 3). The most common complication was urinary retention (16%). The wound infection rate was 11%, and anastomotic leaks occurred in 5% of patients (26 of 502). Criteria for wound infections included any sign of infection (purulence or cellulitis) either of the abdominal or perineal wound for 30 days after surgery. The anastomotic leak rate for low, middle, and high rectal and rectosigmoid cancers was 2.9%, 2.4%, 2.8%, and 6.2% respectively. Reoperations for in-hospital complications were performed in 27 patients. The overall postdischarge complication rate was 15% (77 of 514). The most frequent complications were small bowel obstruction secondary to nonmalignant adhesions (5.8%),

Table 1. PREOPERATIVE COMORBID CONDITIONS

Condition	n	%
Hypertension	147	28.6
Diabetes mellitus	51	9.9
Coronary artery disease	51	9.9
COPD	38	7.4
Carcinoma*	33	6.4
Arrhythmias	23	4.5
Myocardial infarction	20	3.9
Cerebrovascular accident	16	3.1

COPD = chronic obstructive pulmonary disease.
* Patients with a history of another carcinoma but free of disease for last 4 years or more.

Table 2. SYMPTOMS AT THE TIME OF PRESENTATION (N = 514)

	n	Stage I (n = 272)	Stage II (n = 111)	Stage III (n = 63)	Stage IV (n = 68)	Total % (n = 514)
None	84	53	14	8	8	16
Bleeding	315	175	71	38	31	61
Change in bowel habits	171	66	57	19	29	33
Pain	68	32	13	7	16	13
Weight loss	52	13	16	10	13	10
Others	17	2	6	4	5	3
Anemia	12	2	2	5	3	2
Obstruction	6	1	2	1	2	1

parastomal hernias (6.4%; 30 of 235) and nonmalignant strictures (1.6%) (Table 4).

Long-Term Outcomes

At last follow-up, 280 patients (54%) were alive and 234 (46%) were dead. Of the 446 patients undergoing curative surgery, recurrence of any type was diagnosed in 100 (22%); 338 patients (76%) remained free of disease. The disease status was uncertain in eight patients (2%). Treatment for recurrent tumor was surgery alone in 17%, surgery plus additional chemotherapy, radiation therapy, or both in 21%, only radiation therapy, chemotherapy, or both in 32%, and no treatment in 16%. Thus, 70% (70 of 100) of the patients with recurrent disease received some kind of treatment, and 17% (15 of 86) of these patients were in turn free of disease at the final follow-up.

Survival and Recurrence

The overall 5-year survival rate was 64% (Fig. 2) and the disease-free survival rate was 79%. Stage-specific survival rates for all patients are shown in Figure 3. The probability of developing a recurrence of any type at 5 years was 21%. The 5-year overall survival and disease-free survival rates, probability of recurrence, and patterns of recurrence for different stages, stratified according to procedures done, are given in Table 5. The recurrence rate was high and the survival short for patients in the "other operation" group, principally because most were Hartmann procedures for stage IV rectal cancer or proctocolectomy and ileorectostomy for ulcerative colitis complicated by a rectal cancer.

Overall, the local recurrence rate for all stages and all operations was 7% (Fig. 4). Stage-specific local recurrence rates are shown in Figure 5. The 5-year disease-free survival rate was 79%. Thus, 21% of patients actually failed the operation in that they had a local or a distant recurrence (or both).

AR had a local recurrence rate of 7% and a disease-free survival rate of 78% for all patients and stages. The local recurrence rate in stage III disease was higher (13%) than that achieved by APR (7%) and CAA (0%).

Patients after CAA had a local recurrence rate of 6% for

Table 3. IN-HOSPITAL COMPLICATIONS

Organ System	Complication	n	%
Infectious	Wound infection*	58	11.3
	Urinary tract infection	34	6.6
	Pyrexia	12	2.3
	Pneumonia	6	1.2
Pulmonary	Atelectasis	17	3.3
	Respiratory failure	3	0.6
Cardiovascular	Ischemic cardiac event	22	4.3
	Arrhythmia	11	2.1
	Pulmonary embolism	6	1.2
Genitourinary	Urinary retention	84	16.3
Gastrointestinal and local	Anastomotic leak†	16	5.4
	Prolonged ileus	31	6.0
	Small bowel obstruction	10	1.9
	Hemorrhage	6	1.2

* Wound infection includes abdominal and perineal wounds.
† The denominator is 294 because of the number of anastomoses.

Table 4. POSTDISCHARGE COMPLICATIONS

	n	%
Fistula	5	1.0
Impotence	3	0.6
Incisional hernia	1	0.2
Parastomal abscess*	1	0.4
Parastomal hernia*	15	6.4
Sinus	1	0.2
Small bowel obstruction	30	5.8
Stomal bleed*	1	0.4
Stomal necrosis*	1	0.4
Stool incontinence†	3	1.0
Stricture	8	1.6
Urine incontinence	1	0.2
Volvulus	1	0.2

* Denominator is 235 (number of stomas).
† Denominator is 294 (number of anastomoses).

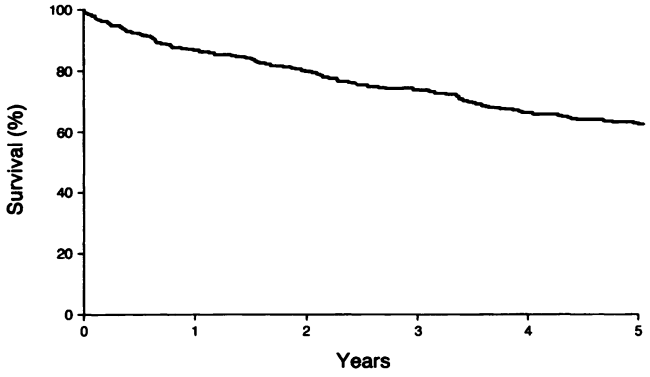

Figure 2. Overall 5-year survival rate for all patients (n = 514), all stages, all operations.

all patients and stages and 0% for stage III disease; however, this group was small.

APR was associated with a local recurrence rate of 4% for all patients and stages; for stage III disease specifically, it was only 7%. Figure 6 details operation-specific 5-year survival figures; the outcomes of AR, CAA, and APR were nearly identical. Figure 7 details operation-specific local recurrence rates; all procedures resulted in few local recurrences.

Table 6 shows the patterns of failure, including local failure only, distant failure only, and local plus distant, by operation performed. The predominant mode of failure for all operations was distant failure alone. The 5-year probabilities of failure when analyzed as "local only" and "local first" were 6% and 7%, respectively, for all patients.

Analysis of determinants of survival and recurrence are presented in Tables 7 and 8, respectively. On univariate analysis, tumor size, depth of penetration of tumor, involvement of lymph nodes by tumor, and presence of metastasis were found to be statistically significant for overall survival as well as for tumor recurrence. Age and sex of the patient, grade of tumor, presence of comorbid conditions, and absence of an anastomosis were found to be significant for overall survival only.

On multivariate analysis, depth of penetration by tumor (lateral extent), number of lymph nodes involved by tumor, and presence of distant metastasis were found to be associated with decreased survival and increased recurrence. Age, sex, comorbid conditions, and presence of a stoma were associated with survival only.

Table 5. OVERALL AND STAGE-SPECIFIC SURVIVAL AND RECURRENCE FOR ALL PATIENTS AND BY TYPE OF OPERATION PERFORMED

	Overall (% of patients)	Stages (% of patients) I	II	III	IV
All patients (n = 514)					
Survival	64	85	65	34	5
Disease-free survival	79	88	66	60	—
Local recurrence	7	4	9	10	—
Recurrence any site	21	12	34	40	—
Anterior resection					
Survival	69	87	68	35	9
Disease-free survival	78	89	65	57	—
Local recurrence	7	3	11	13	—
Recurrence any site	22	11	35	43	—
Coloanal anastomosis*					
Survival	79				
Disease-free survival	83				
Local recurrence	6				
Recurrence any site	17				
Abdominoperineal resection					
Survival	67	84	63	27	7
Disease-free survival	80	86	73	56	—
Local recurrence	4	4	0	7	—
Recurrence any site	20	14	27	44	—

* Low patient numbers preclude meaningful analysis.

DISCUSSION

We found that local recurrence was low and survival reasonably long in patients treated by appropriate "tumor-

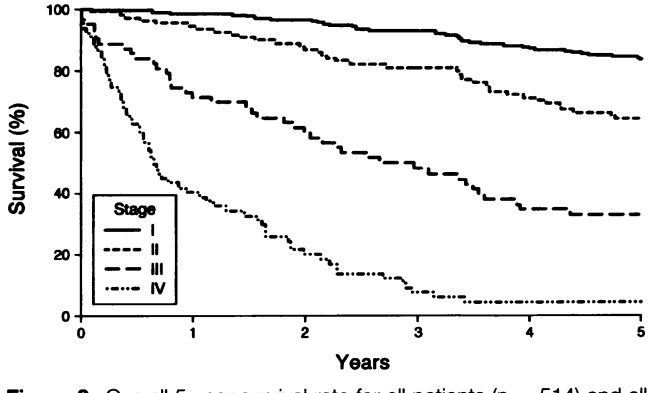

Figure 3. Overall 5-year survival rate for all patients (n = 514) and all operations by stage of disease.

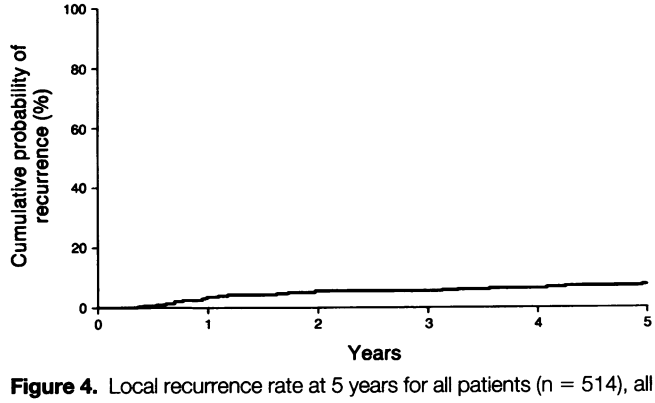

Figure 4. Local recurrence rate at 5 years for all patients (n = 514), all stages, all operations.

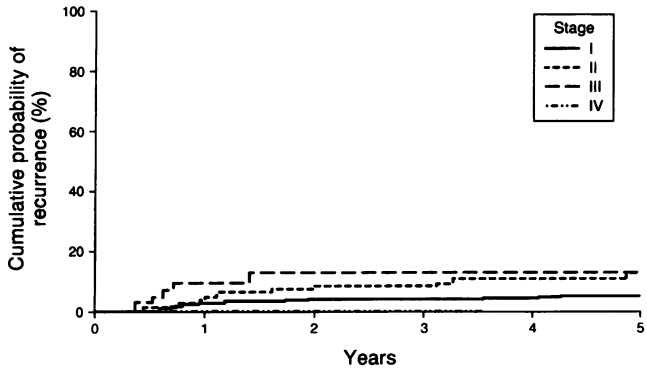

Figure 5. Local recurrence rate at 5 years for all patients (n = 514) and all operations by stage of disease.

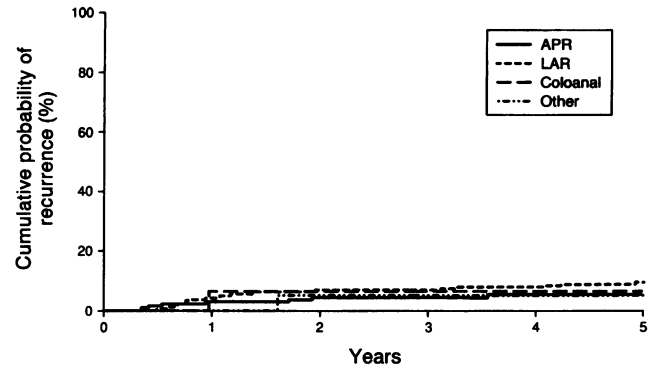

Figure 7. Local recurrence rate at 5 years for all patients (n = 514) and all stages by operation performed.

specific" mesorectal excision. Moreover, these outcomes were achieved with low morbidity and mortality rates.

Surgical technique plays an immensely important role in the management of rectal cancer. McCall et al.[8] and we[9] have documented a wide range of recurrence rates after surgery alone for rectal cancer. The best results in terms of local recurrence have been achieved using a technique termed total mesorectal excision. This technique is best described as removal of the envelope of supporting structures that encompass the rectum from the sacral promontory to the pelvic floor. Heald and Ryall,[4] MacFarlane et al.,[5] Enker et al.,[6] and Holm et al.[10] have reported superbly low local recurrence rates using these techniques. The review by McCall et al.[8] supports this observation.

However, total mesorectal excision may not be appropriate for all patients because it is associated with a high leakage rate (≥17%) and the need for routine proximal diversion. To excise all the mesorectum, even for tumors high in the rectum, may condemn patients to a leak and thus the need for a diverting stoma. In response to this problem, some authors are starting to report performing routine CAA after total mesorectal excision. A rectal cancer operation that mandates a stoma or a CAA to eliminate the risk of leakage, because all the mesorectum has been excised, no matter what the location of the tumor, seems unnecessary.

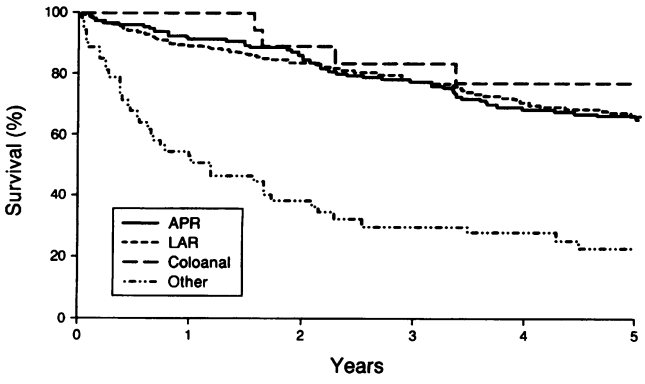

Figure 6. Overall 5-year survival rate for all patients (n = 514) and all stages by operation performed.

Local metastatic deposits of tumor in lymph nodes rarely if ever extend 5 cm below the most distal margin of tumor.[11–15]

The concept of appropriate "tumor-specific" mesorectal excision may be a more reasonable surgical strategy, especially because functional outcome after sphincter-sparing operation depends on the level of the anastomosis above the pelvic floor: the higher the anastomosis, the better the function.[16–18] The data from the present study, as well as from our previous report,[7] suggest that "tumor-specific" mesorectal excision yields results no different from those of total mesorectal excision, but at lesser cost in terms of leakage and death. Such an approach tailors the operation to the tumor, attempting to save as much rectum as possible to achieve good function.

Because the local recurrence rates reported here are so low, a policy of routine adjuvant radiation therapy for stage II and some stage III cancers,[19] if resected by APR, may not be indicated. However, the local recurrence rates of 11% and 13% after low AR in stage II and III disease, respectively, argue for continued local adjuvant radiation management in these patients. Indeed, because local recurrence rates were reported to be high in several series in the past, prospective randomized trials of radiation and chemotherapy were begun to "salvage" surgical outcomes. The GTISG1 and NCCTG2 trials and others[20,21] showed significant improvement in the rates of local recurrence and

Table 6. PATTERNS OF FAILURE FOR ALL PATIENTS AND BY OPERATION PERFORMED (N = 514)

	All	APR	LAR	Coloanal	Other
n		169	272	19	54
None	338	121	184	15	18
Local	29	6	21	1	1
Distant	49	19	27	1	2
Local and distant	11	4	5	1	1

APR = abdominoperineal resection; LAR = low anterior resection.

Table 7. OVERALL SURVIVAL FOR DIFFERENT RISK FACTORS

		Univariate Analysis				Multivariate Analysis			
	n	5-yr Survival (%)	Chi Square	RR	p Value	Chi Square	RR	95% CI	p Value
Age									
≤65 yr	218	80	43.3	2.7	0.0001	41.5	2.80	2.05–3.87	0.0001
>65 yr	242	58							
Sex									
Male	277	67	4.0	0.7	0.04	4.8	0.71	0.52–0.96	0.02
Female	183	71							
Comorbid condition									
No	195	71	3.9	1.3	0.04				
Yes	265	67							
Size									
0–5 cm	328	74	20.6	1.9	0.0001				
>5 cm	123	55							
Grade									
1–2	378	71	7.1	1.6	0.008				
3–4	82	55							
Depth of tumor invasion									
T1	58	88	81.3	1.0	0.0001				
T2	224	81		1.5					
T3	164	50		3.4		8.86	1.63	1.18–2.26	0.002
T4	14	7		10.8		6.92	2.53	1.26–5.05	0.008
Number of nodes involved									
0	372	79	215.6	1.0	0.0001				
1–3	58	33		3.8		25.49	2.87	1.90–4.32	0.0001
>3	29	7		10.2		51.02	6.43	3.86–10.73	0.0001
Metastasis status									
M0	420	74	197.8	8.2	0.0001				
M1	40	8				46.12	4.78	3.04–7.50	0.0001

RR = relative risk; CI = confidence interval.

5-year survival in patients treated with chemotherapy and radiation therapy *versus* either surgery alone or radiation alone; however, the benefit of such aggressive management appeared to depend on high baseline recurrence rates for surgery alone. Indeed, if the baseline recurrence rate is 20% to 30%, then adjuvant chemotherapy and radiation therapy probably need to be performed to salvage these poor results of surgery alone. But if the local recurrence rate is low (<5% to 10%), the utility of attempting to decrease it further by aggressive and sometimes morbid chemotherapy and radiation therapy may demand the treatment of huge numbers of patients to achieve any meaningful decrease in recurrence; thus, it may not be justified.

Moreover, radiation therapy hinders function after anterior resection.[22] We showed that the number of stools per day, clustering, night stools, fecal incontinence, need to wear a pad, perianal skin irritation, use of hypomotility agents (Lomotil®), liquid stools, and inability to defer defecation were all increased significantly in patients radiated after AR *versus* those who were not.[22] Whether such adverse function might be mitigated by preoperative radiation therapy is unknown. One study that looked at preoperative radiation and postoperative function showed that high-dose preoperative radiation therapy decreased postoperative anal sphincter pressures, decreased neorectal capacity, and caused worse bowel function than in patients who had received low-dose or no preoperative radiation therapy.[23] The future of preoperative radiation therapy lies in the ability to stage patients accurately to reduce the chance of radiating potentially large numbers of patients unnecessarily.

Although the recurrence rates reported here are low and question the need for local adjuvant radiation treatment, the disease-free survival rate of the entire group was only 79%; 21% of the patients had recurrent disease by 5 years. Recurrence of tumor at sites removed from the pelvis was common. Among all patients, 34% of stage II and 40% of stage III patients had a recurrence: only 10% recurred locally, but 30% recurred distantly. It seems appropriate, therefore, that systemic adjuvant therapy for appropriate tumors is indicated to reduce recurrence outside of the pelvis and to enhance survival. Clearly, the low local recurrence rate did not eliminate deaths from rectal cancer, either in our patients or in any other study reported to date.

Table 8. PROBABILITY OF RECURRENCE AT 5 YEARS FOR DIFFERENT RISK FACTORS

		Univariate Analysis				Multivariate Analysis			
	n	5-yr Probability	Chi Square	RR	p Value	Chi Square	RR	95% CI	p Value
Age									
≤65 yr	196	17	4.7	1.6	0.03	5.75	1.7	1.10–2.65	0.01
>65 yr	213	25							
Size									
0–5 cm	302	17	17.4	2.4	0.0001				
>5 cm	99	34							
Depth of tumor invasion									
T1	58	7	98.6	1.0	0.0001				
T2	215	14		1.8					
T3	126	35		5.0		15.37	2.5	1.58–4.00	0.0001
T4	10	100		27.6		50.8	17.2	7.87–37.60	0.0001
Metastasis									
No	405	20	47.0	14.4	0.0001				
Yes	4	100				22.29	13.6	4.60–40.18	0.0001
Number of nodes involved									
0	361	19	24.8	1.0	0.0001				
1–3	37	34		2.3		3.88	1.88	1.00–3.55	0.04
>3	11	61		5.3					

RR = relative risk; CI = confidence interval.

In this study, multivariate analysis linked recurrence and survival to stage of tumor: the higher the stage, the worse the recurrence and survival rates. This association was strong ($p < 0.0001$) and not surprising. What was reassuring was that recurrence and survival were not linked to the type of surgery performed. Stage for stage, APR, AR, and CAA had similar rates of local recurrence and 5-year survival. What is implied in these results is that the techniques used did not differ between the procedures: total excision of the envelope of supporting structures around the rectum for low and middle rectal tumors, no matter if continuity was established (low AR, CAA) or not (APR), had uniform outcomes. These results extend and confirm those of Wilson and Beahrs,[7] who found that adequate margins, carefully achieved, yielded a low local recurrence rate and good survival.

In conclusion, appropriate "tumor-specific" excision of the rectum and supporting structures minimized complications and appeared to achieve a low rate of local recurrence and a 79% 5-year survival rate in patients with rectal cancer. For patients undergoing AR for tumors high in the rectum, 5-cm margins of bowel, mesorectum, and supporting structures were attained; leak rates were low and diverting stomas were not required. For patients with tumors located in the middle to low rectum, complete excision of the envelope of supporting structures, including the mesorectum and lateral structures, followed by low AR, CAA, or APR was performed. The low local recurrence rates achieved in stage I, stage II, and some stage III tumors question the need for the routine adjuvant radiation therapy to the pelvis currently given to some stage II and III patients. In contrast, the 79% 5-year disease-free survival rate and the systemic recurrence rate of up to 30% to 40% argue strongly for systemic adjuvant treatment to enhance survival.

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Discussion

DR. EDWARD M. COPELAND, III, (Gainesville, Florida): I know you-all are probably getting tired of hearing from me, but I'm sort of a captive audience up here, and everybody knows it, so they send me their papers to review.

Having said that, I could spend about an hour discussing this particular paper. Congratulations, Dr. Pemberton. This is excellent work.

The authors have modified the total mesorectal excision to "tumor specific" mesorectal excision, and I agree. Several investigators have determined the maximal distance of distal nodal spread for high rectal lesions to be less than 5 cm. For lesions of the middle and lower rectum total mesorectal excision should be done.

In my practice, I have employed both preoperative radiation therapy and the tailored mesorectal excision described by Dr. Pemberton. The question is, does the patient need both a total mesorectal excision and neoadjuvant therapy? No study exists to answer the question and surgical techniques vary so dramatically among different surgeons that the study may be difficult unless done in a single institution.

There are now at least three randomized prospective trials that demonstrate an improvement in both local recurrence and survival with the use of preoperative radiation therapy compared to surgery alone. In our series of 190 patients treated with preoperative radiation therapy, all were initially Stage II or Stage III. Patients downstaged to a pathologic T0 or T1 had a 93% 5-year survival, and those downstaged to a pathologic T2 had an 83% 5-year survival.

Thus, our series is not comparable to the Mayo Clinic's study because of downstaging from radiation therapy that correlated with an improvement in 5-year survival. Also, several of the patients in our series downstaged to pathologic T0 had a successful transanal local excision. For the time being, I will continue to treat the patient who has a bulky circumferential lesion clearly invading in the pericolic fat with preoperative radiation therapy now combined with intravenous 5-fluorouracil followed by a tailored mesorectal excision. For patients with smaller lesions in whom a mesorectal excision will predictably eliminate all pelvic disease, no radiation therapy is indicated.

Radiation therapy is utilized at the Mayo Clinic, since 418 patients were eliminated from this study because they received it. Dr. Pemberton, what are the indications for the use of radiation therapy possibly combined with chemotherapy at your institution? I assume all patients received the tailored mesorectal excision that you describe. [Applause]

DR. KEITH D. LILLEMOE (Baltimore, Maryland): Thank you, Dr. Wells, Dr. Copeland, Members of the Association. I'd like to congratulate Dr. Pemberton and his colleagues at the Mayo Clinic for this very nice presentation.

The conclusions of this paper, in my mind, are that with an adequate cancer operation, resecting the appropriate component of the mesorectum, that a low incidence of local recurrence can be seen, perhaps obviating the need for radiation therapy at a low rate of complications such as anastomotic leak, which can be seen in some of the more aggressive, radical resections of the rectal mesentery.

I have a few questions concerning points that were raised in your manuscript as well as in your presentation. First of all, John, in your manuscript, you somewhat balk at the suggestion that for stage II and III rectal cancers treated by low anterior resection in which you specifically, although not shown here, cited a local recurrence rate of 11% to 13%, you balk on the conclusion that maybe radiation therapy is not indicated in this group. And I would like to know your current policy with respect to use of adjuvant radiation therapy at the Mayo Clinic.

In follow-up to what Dr. Copeland said, we see that during the same time period over 400 patients did get radiation chemotherapy at your institution or back at your home institutions, and I wonder what were the criteria which you chose to use radiation chemotherapy during the time period of this study? Were there any selection factors that could have biased this outcome?

My second question is that I was very impressed with your results with respect to two late complications. One, the anastomotic stricture rate, which you did not show today but reported in the paper, was only 1.6%, which I think is excellent, presuming that you used a stapled anastomosis in a number of these low anterior resections. The incidence of impotence was only .6%.

My personal results in this population of mostly older males would be a higher incidence of both of these conditions. I'd like to have you perhaps better define how you identified these complications. And since it really is this low, could you give any pointers to myself and the other members of the group regarding how you obtained such excellent results.

My next question relates to the timing of your series. All the